REMARKS

Claims 59-88 are pending. In this communication, Applicants have amended Claims 59, 61, 62, 67, 69, 74, 76-78, and 80-83. The concept of partial deletion of the endogenous adenoviral promoter is supported at least in paragraph 0104 of the published application. No new matter is introduced. Allowance of all pending claims is respectfully requested.

In the Office Action of March 15, 2005, the Examiner set forth a number of grounds for objection and rejection. These grounds are addressed individually and in detail below.

Sequence compliance

The Examiner indicates that some of the nucleotide sequences in the specification are not identified by sequence identifier numbers. Applicants have amended the specification to provide a sequence identifier number for each sequence disclosed in the specification.

Claim objections

Claims 67, 69, 82 and 83 are objected to for using abbreviations. Claims 67, 69, 82 and 83 have been amended to spell out each abbreviation for clarity.

Double Patenting

Claims 59-87 stand rejected under the judicially created doctrine of obvious type double patenting over U.S. Patent No. 6,692,736. Applicants have included a Terminal Disclaimer for U.S. Patent No. 6,692,736 to obviate the ground of the rejection. Withdrawal of the double patenting rejections to Claims 59-87 is respectfully requested.

Rejections under 35 U.S.C. § 112

Claims 61, 67-71, 81 and 82 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reasons stated on pages 6-7 of the Office Action. The Examiner states that there is insufficient antecedent basis for the term "said adenovirus" in Claim 80. It thus appears that the 35 U.S.C. § 112 rejection was raised against Claims 61, 67-71, 80 and 81. Applicants have amended Claims 61, 67, 70, 80 and 81 to obviate the grounds for rejection. Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph is respectfully requested.

Rejections under 35 U.S.C. § 102

Claims 59-62, 65, 67-70, 72, 74-78, 80, 81 and 84-87 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Chang et al. (WO 99/25860) for reasons stated on pages 7-8 of the Office Action.

For anticipation under 35 U.S.C. § 102, the reference "must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present." (MPEP §706.02). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a

single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Independent Claim 59, as amended, is directed to a replication-competent adenoviral vector for selective cytotoxicity of a target cell. The adenoviral vector comprises first and second genes co-transcribed as a single mRNA wherein the first and second genes are under transcriptional control of a heterologous, target cell-specific transcriptional regulatory element (TRE). The first gene is an adenoviral gene and the second gene has a mutation or partial deletion of its endogenous promoter and is under translational control of an internal ribosome entry site (IRES).

Chang et al. generally describes cell-specific expression vectors, including adenovirus vectors that comprise a gene under the control of a tissue specific promoter. Chang et al. describe and exemplify adenoviral constructs wherein the gene product of one gene drives transcription of further genes(s). For example, the first gene (i.e., E1a) has its promoter deleted, the entire second gene is present (i.e., E1b) and the genes are linked by an IRES. In other words, the Chang et al. constructs have the coding region of a first gene (promoter deleted) and an entire second gene linked by an IRES. (See page 18 and Example 1.) Further, Chang et al. do not describe a partial deletion or mutation of the endogenous promoter of the second co-transcribed gene.

The Office Action states that Chang discloses "the first gene has a mutation in the transcriptional regulatory region, which comprises promoters and enhancers," and the bridging paragraph on pages 17-18 and paragraph 2 on page 18 of Chang is cited as support. Applicants respectfully submit that the cited paragraphs describe vectors in which the native transcriptional regulatory sequence of the first gene is "completely

deleted" (see e.g., page 18, lines 2-3 and line 18) and do not mention constructs where the native transcriptional regulatory sequence of the second gene has a partial deletion or mutation.

Claims 60-62, 65, 67-70, 72, 74-78, 80, 81 and 84-87 are not anticipated by Chang because they depend from Claim 59. Accordingly, withdrawal of the 35 U.S.C. § 102(a) rejection is respectfully requested.

Rejections under 35 U.S.C. § 103

Claims 63, 64, 66 and 73 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chang in view of Yu et al. (Cancer Research, 1999) or Lin et al. (PNAS, 1995), or Roelvink et al., (US2001/0047081) for reasons stated on pages 8-10 of the Office Action.

Claims 71 and 79 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chang in view of Perez and White (JCB, 1998) for reasons stated on pages 10-11 of the Office Action.

Claims 82 and 83 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chang in view of Stein et al. (MCB, 1998) or Borman et al. (NAR, 1995) for reasons stated on pages 11-12 of the Office Action.

To establish a *prima facie* case of obviousness the prior art reference (or references when combined) must teach or suggest all of the claim limitations. In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991) and MPEP § 2142. Moreover, obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to

do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art (see MPEP 2143.01; In re Fine, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 21 USPQ2d 1941 (Fed. Cir. 1992)).

As discussed above, Chang et al. does not teach or suggest a replication-competent adenoviral vector for selective cytotoxicity of a target cell which has a partial deletion or mutation of the endogenous promoter of a second co-transcribed gene. Therefore, Chang et al. does not render independent Claim 59 obvious. Yu, Lin, Roelvink, Perez, Stein, and Borman do not cure the deficiency of Chang et al.. More specifically, Yu describes the hK2 promoter and enhancer; Lin teaches the urothelial promoter; Roelvink discloses the use of an E2F promoter in prostate cancer cells; Perez describes using Fas as a cytotoxic gene in an adenoviral vector in which E1B 19K is deleted; Stein teaches the isolation and utilization of the VEGF IRES; and Borman compares the activity of variety of IRES sequences. None of these references teaches or suggests a replication-competent adenoviral vector for selective cytotoxicity of a target cell which has a partial deletion or mutation of the endogenous promoter of a second co-transcribed gene. Accordingly, Applicants respectfully submit that Chang, Yu, Lin, Roelvink, Perez, Stein, and Borman individually or in combination, do not render Claim 59 obvious.

If an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious. In re Fine, 5 USPQ2d 1596 (Fed Cir. 1988). Accordingly, dependent Claims 63, 64, 66, 71, 73, 79, 82 and 83 are patentable because

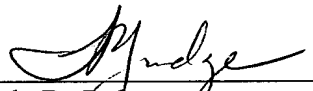
they depend from Claim 59 and define additional patentable subject matter. Withdrawal of the 35 U.S.C. § 103 rejection is respectfully requested.

Conclusion

In light of the above, Applicants submit that this application is now in condition for allowance and therefore request favorable consideration. If any issues remain which the Examiner feels may be best resolved through a personal or telephonic interview, the Examiner is respectfully requested to contact Applicants' counsel, Linda R. Judge at (415) 836-2586.

Respectfully submitted,

DLA PIPER RUDNICK GRAY CARY US LLP



Linda R. Judge
Registration No. 42,702

1200 Nineteenth Street, N.W.
Washington, D.C. 20036-2412
Telephone No. (202) 861-3900
Facsimile No. (202) 223-2085